

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 689290.192	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/US04/19286	International filing date (day/month/year) 17 June 2004 (17.06.2004)	Priority date (day/month/year) 20 June 2003 (20.06.2003)	
International Patent Classification (IPC) or national classification and IPC IPC: G01N 33/48( 2006.01);C12Q 1/68( 2006.01) USPC: 702/29;435/6			
Applicant PAUL E. YOUNG			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of ___ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 18 January 2005 (18.01.2005)		Date of completion of this report 24 March 2006 (24.03.2006)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Marjorie Moran Telephone No. (571)272-1600	

Form PCT/IPEA/409 (cover sheet)(April 2005)

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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## Box No. I Basis of the report

1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into English, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4(a))
  - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- ☒ the international application as originally filed/furnished
- ☒ the description:  
pages 1-30 as originally filed/furnished  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the claims:  
pages 31-35 as originally filed/furnished  
pages\* NONE as amended (together with any statement) under Article 19  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the drawings:  
pages NONE as originally filed/furnished  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 6,9,10 and 17-32

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 6,9,10 and 17-32

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

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**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>11-13</u>	YES
	Claims <u>1-5, 7-8, 14-16</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-5, 7-8, 11-16</u>	NO
Industrial Applicability (IA)	Claims <u>1-5, 7-8, 11-16</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and Explanations (Rule 70.7)  
Please See Continuation Sheet

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

## V. 2. Citations and Explanations:

Claims 1, 3-5, 7-8, and 16 lack novelty under PCT Article 33(2) as being anticipated by Natsoulis, US 20030180808.

Claims 1 is directed to a method for identifying a compound with a selected activity comprising determining a change in expression profile of a selected set of genes in the presence and absence of a first compound, determining a change in expression profile for a second compound, and comparing changes in expression profiles. Natsoulis discloses a method for generating a group of compounds having related activities comprising steps of determining a change in expression profiles of a set of selected genes (*e.g.*, providing a selected drugs, contacting each compound with a subject cell, measuring the expression response, [0015-0018] and claims 1, 11, and 12), comparing changes of expression compounds [0018]. Natsoulis discloses determining a change of expression profiles in the presence and absence of a first and a second compound ([0015-0018], [0035], claim 1 and fig. 3). Thus, Natsoulis anticipates claim 1. Natsoulis discloses genes present in a cell and are part of a genome [0120] (*e.g.*, compounds were administered to rats), thus anticipates claims 3 and 16. Natsoulis discloses measuring transcription, and specifically synthesis of RNA [0035, 0121], thus anticipates claims 4-5. Natsoulis discloses physiological changes in a cell [0033], thus anticipates claim 7. Natsoulis discloses therapeutic activity of compounds [0033], thus anticipates claim 8.

Claims 1-5, 7-8, and 14-16 lack novelty under PCT Article 33(2) as being anticipated by Bristow, WO 03/023066.

Bristow discloses a method of identifying genes involved in a disease comprising obtaining gene expression profile from healthy and affected individual subjected to a therapy or placebo, and comparing a change in expression profiles (p. 3, line 5-29, p. 5, line 1-22, example 1). Thus, Bristow anticipates instant claim 1. Bristow discloses antioplastic activity (cancer as a disease stage and an agent for treatment, p. 3, line 20), thus anticipates claim 2. Bristow discloses a set of genes present in a cell (a human body, tissue, p. 3, line 7-8 and p. 5, line 16-21), thus anticipates claims 3 and 16. Bestow discloses measuring expression profiles such as transcription profile and synthesis of RNA (p. 5, line 16-22), thus anticipates claims 4-5. Bestow discloses physiological changes in a cell (p. 5, line 1-3), thus anticipates claim 7. Bestow discloses therapeutic activity of compounds (see p. 34-43 for agents), thus anticipates claim 8. Bestow

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Supplemental Box

discloses myocytes transformed with an expression construct comprising a screenable marker gene (p. 5, line 19-22), thus anticipates claims 14-15.

Claims 2 and 12-13 lack of an inventive step under PCT Article 33(3) as being obvious over Bristow, WO 03/023066, in view of Skolnick, U.S. Patent 5,624,819.

Bristow teaches a method of claims 1, 3-5, 7-8, and 16, as set forth above.

Bristow does not teach using colon cells, and specifically cancer cells, for identifying a compound.

Skolnick discloses a method of screening drugs for cancer therapy (e.g., colon cancer, col. 4, line 9-10 and 38, fig. 1D).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Bestow to screen drugs for treatment colon cancer, such as taught by Skolnick, where the motivation would have been to identify drugs for a disease affecting one in every hundred Americans, as taught by Skolnick (col. 2, line 34).

Claims 2 and 12-13 lack of an inventive step under PCT Article 33(3) as being obvious over Bristow, WO 03/023066, in view of Wang, U.S. Patent 6,617,335.

Bristow teaches a method of claims 1, 3-5, 7-8, and 16, as set forth above.

Bristow does not teach using camptothecine compounds.

Wang discloses anti-cancer compounds and a method for increasing the intracellular concentration of a drug. Wang discloses camptothecine drugs selected for treatment of cancer (col. 3, line 38-49).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Bestow to screen for camptothecine drugs effective for treatment cancer, such as taught by Wang, where the motivation would have been to overcome drugs toxicity in cancer affecting individuals, as taught by Wang (col. 2, line 47-59).

Claims 1-5, 7-8, and 11-16 meet the criteria set out in PCT Article 33(4), and thus have industrial application because the subject claimed can be made or used in industry for identifying therapeutically important compounds for treating affected individuals.